REMARKS

This application contains claims 1-83, the status of which is as follows:

(a) Claims 9, 11, 12, 27, 46, 60, and 74 have been currently cancelled without prejudice.

(b) Claims 4-6, 14, 15, 30-32, 41, 42, and 47-49 are as originally filed.

(c) Claims 1-3, 7, 8, 10, 13, 16-26, 28, 29, 33-35, 44, 45, 58, 59, 72, and 73 have been currently amended.

(d) Claims 36-40, 43, 50-57, 61-71, and 75-77 were previously presented.

(e) Claims 78-83 are new.

No new matter has been added.

Claim rejections under §112

Claims 1-77 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Applicants respectfully traverse the rejection of claim 1. The Examiner wrote, "It is unclear how **the same site** can have stimulation from two subsets of electrodes, presumed to be different. . ." (emphasis in original). Applicants respectfully submit that one of ordinary skill in the art would understand a "site" in this context as meaning a general place, rather than a single point, as apparently argued by the Examiner. Moreover, a "site" cannot be understood to mean a point, because it is not possible to implant even a single electrode at a single, infinitely small point.

In addition, this interpretation of "site" is supported by originally-filed dependent claims 7 and 8, which depended from claim 1. It is clear in these claims that the stomach and antrum are two possible "sites" at which the electrodes may implanted. These claims as originally filed read (emphasis added):

> 7. The apparatus according to claim 1, wherein the implantation site includes a stomach of the patient, and wherein the set of electrodes are adapted to be fixed to the stomach.
>
> 8. The apparatus according to claim 1, wherein the implantation site includes an antrum of a stomach of the patient, and wherein the set of electrodes are adapted to be fixed to the antrum.

Thus, it is clear that the recited "site" is large enough to implant two subsets of electrodes.

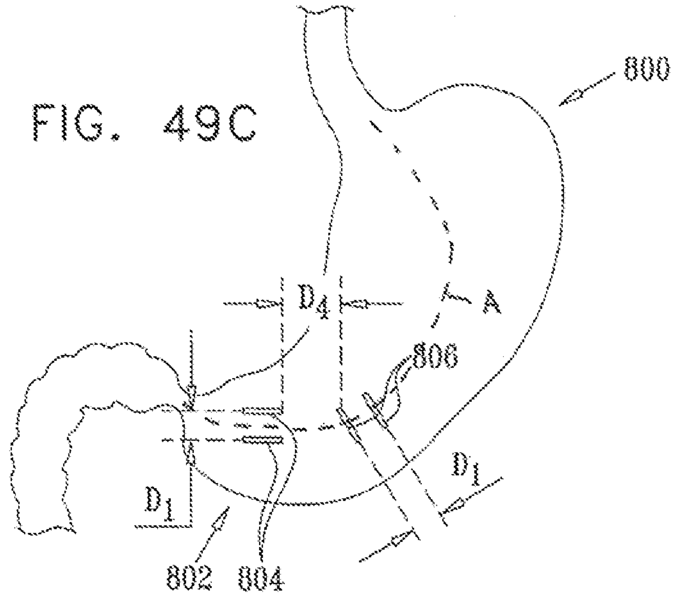
Applicants thus respectfully submit that claim 1, as well as the claims that depend therefrom, are allowable under 35 U.S.C. §112, second paragraph. (Applicants also note that the two subsets are not necessarily different; see dependent claim 5.)

Regarding claims 16-21, 33-35, and 36-77, the Examiner argued that the phrase "axis of the stomach" is indefinite because "there are infinite axes of any structure, the axis must be in relation to something in order to have any useful meaning." While not necessarily agreeing, Applicants have amended the phrase throughout the claim set to recite a "<u>curved long</u> axis of the stomach." This addition is supported in Figs. 49A-C and paragraphs [0673]-[0677] of the specification as originally filed (as published as U.S. Patent Application Publication No. 2009/0088816). The specification states that the longitudinal and perpendicular orientations of the electrodes with respect to the axis should be understood as shown in these figures:

> FIG. 49A is a schematic illustration of an anterior antrum 802 of a stomach 800, having implanted thereon two pairs of longitudinally-oriented electrodes 804.... **In the context of the present patent application and in the claims, this orientation of electrodes on the stomach is referred to as a "longitudinal orientation with respect to the axis of the stomach."** ([0673]; emphasis added)
>
> FIG. 49B is a schematic illustration of anterior antrum 802, showing two pairs of perpendicularly-oriented electrodes 806, in accordance with an embodiment of the present invention.... **In the context of the present patent application and in the claims, this orientation of electrodes on the stomach is referred to as a "perpendicular orientation with respect to the axis of the stomach."** ([0674]; emphasis added)
>
> FIG. 49C is a schematic illustration of anterior antrum 802, showing one pair of longitudinally-oriented electrodes 804 and one pair of perpendicularly-oriented electrodes 806.... **In the context of the present patent application and in the claims, an orientation of electrodes on the stomach combining at least one longitudinal electrode and at least one perpendicular electrode is referred to as a "mixed orientation with respect to the axis of the stomach."** ([0676]; emphasis added)

It is clear from the orientations of the various electrode sets shown in the figures and from the passages cited above that the "axis" is the curved long axis of the stomach, as shown in the following marked-up version of Fig. 49C, in which the dashed line A illustrates the axis (the figure as originally filed does *not* include the dashed line A):

FIG. 49C

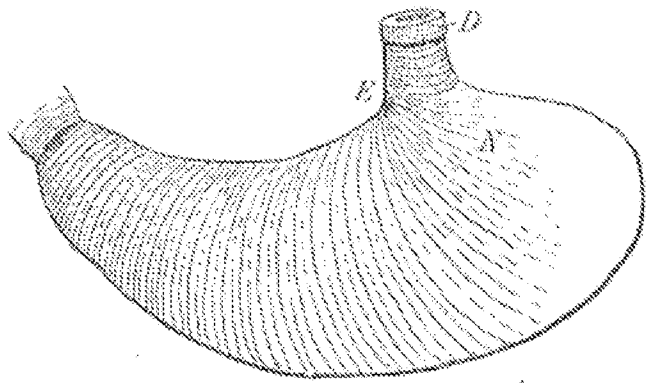


As can be clearly seen, "longitudinally-oriented electrodes 804" are oriented longitudinally, i.e., substantially parallel, to the curved axis of the stomach, and "perpendicularly-oriented electrodes 806" are oriented substantially perpendicular to the curved axis of the stomach. The additional qualifier "long" has been added to preclude misunderstanding the phrase as referring to some other, non-intended axis of the stomach.

In addition, the phrase "curved axis" has been used in the art to describe the axis illustrated above. For example, it has been known for over a century that the circular fibers of the stomach are arranged as "larger and larger circles as they surround the body of the stomach at right angles to its curved axis," (emphasis added) as shown in the following drawing[1]:

[1]Birmingham, A., "The arrangement of the muscular fibres of the stomach," Transactions of the Royal Academy of Medicine in Ireland, Springer London (1898), which is attached hereto as Appendix A

{V0066577.1}



In light of these amendments and remarks, Applicants respectfully submit that claims 16-21, 33-35, and 36-77 are allowable under 35 U.S.C. §112, second paragraph.

Applicants respectfully traverse the rejections of claims 23, 26-28, 45-47, 59-61, and 73-75. The Examiner argued regarding these claims that "within this apparatus claim there is no component, electrode or other component which is disclosed as delivery a pacing pulse. . ." (page 4 of the office action). Applicants respectfully disagree. Apparatus claims 23 and 26-28 recite that the "control unit" drives one of the subsets of the set of electrodes to apply the pacing pulse. Claims 45-47, 59-61, and 73-75 are method claims, so this portion of this rejection does not appear to apply to these claims.

The Examiner further argued that "it is unclear how the pacing pulse is delivered, to what structure it is delivered or what it is. There could be a cardiac pacing pulse, or some other kind of pacing pulse. Furthermore, it is unclear what is being paced" (page 4 of the office action). Applicants respectfully submit that the claims, when read in the context of the independent claims from which they depend, clearly recite that the pacing pulse is applied to the site at which the electrodes are implanted. For claims 23 and 26-28, this site is either the stomach or an intestinal site, as now recited in independent claim 22. For claims 45-47, 59-61, and 73-75, this site is the stomach, as recited in independent claims 33, 34, and 35, respectively. Although not believed necessary for patentability, Applicants have nonetheless amended claims 23, 26, 44, 45, 58, 59, 72, and 73 to explicitly recite that the pacing pulse is (or is not) applied to the site recited in the respective parent claims.

Furthermore, the broad concept of applying pacing pulses to the gastrointestinal tract has been known to those skilled in the art for nearly 50 years (see, for example,

Bilgutay AM et al., "Gastro-intestinal Pacing: A New Concept in the Treatment of Ileus," Ann Surg. 1963 September; 158(3): 338–347, which is attached hereto as Appendix B). Therefore, one of ordinary skill in the art would readily understand the meaning of applying pacing pulses to gastrointestinal sites, as recited in these claims. (Although the general concept of gastrointestinal pacing is very old, Applicants believe that the particular applications of pacing recited in the claims are novel and non-obvious.)

Applicants thus respectfully submit that claims 23, 26-28, 45-47, 59-61, and 73-75 are allowable under 35 U.S.C. §112, second paragraph.

While not necessarily agreeing with the rejections of claims 27, 46, 60, and 74, Applicants have cancelled these claims without prejudice to expedite the issuance of a patent on subject matter believed to be allowable, as discussed herein.

Claim rejections under §§102 and 103

Claims 1-7, 9-12, 16-21, 33-39, 50-53, and 64-67 were rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,600,953 to Flesler et al. Claims 13-15, 40-42, 54-56, and 68-70 were rejected under 35 U.S.C. §103(a) as being unpatentable over Flesler et al. in view of U.S. Patent Application Publication No. 2004/0162595 to Foley. Claims 22, 29-32, 42, 43, 48, 49, 57, 58, 62, 63, 71, 72, 76, and 77 were rejected under 35 U.S.C. §103(a) as being unpatentable over Flesler et al. in view of U.S. Patent No. 5,690,691 to Chen et al. Claims 23, 26, 28, 45, 47, 59, 61, 73, and 75 were rejected under 35 U.S.C. §103(a) as being unpatentable over Flesler et al. in view of U.S. Patent No. 5,690,691 to Chen et al., and further in view of U.S. Patent Application Publication No. 2005/0021101 to Chen et al. Claims 27, 46, 60, and 74 were rejected under 35 U.S.C. §103(a) as being unpatentable over Flesler et al. in view of U.S. Patent No. 5,690,691 to Chen et al., and further in view of U.S. Patent Application Publication No. 2005/0021101 to Chen et al., and further in view of U.S. Patent Application Publication No. 2003/0055465 to Ben-Haim et al. Claims 24 and 25 were rejected under 35 U.S.C. §103(a) as being unpatentable over Flesler et al. in view of U.S. Patent No. 5,690,691 to Chen et al., and further in view of Ben-Haim et al.

Claims 1 and 11

Applicants respectfully traverse the rejection of dependent claim 11. While not necessarily agreeing with the rejection of independent claim 1, Applicants have amended claim 1 to further recite the features of dependent claim 11, which has accordingly been canceled. Applicants have additionally amended claim 1 to recite the features of dependent claims 7 and 10 in the alternative, as a Markush group, and to clarify that the first and second signals are different from one another.

In rejecting dependent claim 11, the Examiner argued that the following passage from Flesler disclosed the claimed features:

> For some patients, it is desirable to apply the enhancement signal according to a schedule, whereby constriction of the stomach induces a feeling of satiety at times when the patient might choose to eat but should not be eating. At other times, e.g., when the patient is sleeping, the signal is typically not applied. Alternatively or additionally, the enhancement signal is (a) applied during one or more meals during the day, so as to reduce the patient's appetite during those meals, and (b) removed during meals eaten during the remainder of the day, so as to prevent nutritional deficiencies which might occur in some patients from any inappropriate, excessive use of the signals described herein. (col. 3, lines 14-25)

The Examiner argued that the first half of this passage from Flesler discloses applying a signal not responsive to eating, and the second half of the passage discloses applying the signal responsive to eating.

Applicants respectfully submit that the passage from Flesler describes applying <u>the same "enhancement signal,"</u> rather than the <u>different</u> first and second signals recited in claim 1 as amended, one of which reduces a blood glucose level, and the other of which treats obesity. This passage from Flesler thus fails to teach or suggest a central feature of claim 1 as amended.

Applicants thus respectfully submit that claim 1 as amended is allowable. Claims 2-8, 10, and 13-21 directly or indirectly depend from claim 1, and thus are also in condition for allowance.

Claims 22, 29, and 30

Applicants respectfully traverse the rejection of dependent claim 22, which has been recast in independent form including the features of claim 1, from which claim 22 directly depended. Applicants have additionally amended claim 22 to (a) recite the

features of dependent claims 7 and 10 in the alternative, as a Markush group, (b) to clarify that the first and second signals are different from one another, and (c) to no longer recite that the first frequency component is smaller than the second frequency component, but rather that the first and second frequency components are different from each other; the original feature is now recited in new dependent claim 83, and claim 29 has been amended to depend from claim 83 rather than directly from claim 22.

Although Chen may teach pulsing at different frequencies at different locations on the GI tract, Chen does not teach applying two different signals having different respective frequencies, which signals are configured to produce different effects (blood glucose reduction and obesity treatment), as recited in claim 22. Instead, Chen's signals are applied in a phased relationship to produce together a single effect, namely pacing of the GI tract.

Applicants further respectfully submit that Chen fails to teach or suggest the frequencies of the second frequency component recited in dependent claims 29 and 30. Claim 29 recites that the second frequency component is greater than 10 Hz. In contrast, the greatest frequency taught by Chen is about 0.21 Hz (12.5 cycles per minute = 0.21 cycles per second (Hz)) (col. 9, lines 30-31). Not only is Chen's 0.21 Hz about 98% less than the 10 Hz recited in claim 29, but Chen teaches against pacing at this substantially greater recited frequency. Chen states that the pacing should be performed "with electrical stimulations that have a frequency that is equal to or greater than the natural frequency; approximately 10% greater is preferred and 5-20% greater should provide optimum results" (col. 6, lines 51-54; emphasis added), and the greatest frequency of the GI tract taught by Chen is in "the upper portion of the duodenum [which] has a frequency of approximately 12.5 cpm [cycles/minute]," which equals 0.21 Hz (col. 6, lines 44-45). Claim 30 of the present application recites even greater frequencies, which Chen would have even less reason to use.

Applicants thus respectfully submit that claims 22, 29, and 30 are allowable over Flesler in view of Chen, as are claims 23-28, 31, and 32, which directly or indirectly depend from claim 22.

Claims 16-21 and 33-35

Because the Examiner rejected claims 16-21 and 33-35 under 35 U.S.C. §112, second paragraph, as discussed above, the Examiner did not provide any reasons for the rejections of these claims under 35 U.S.C. §102(b) over Flesler. In light of the amendments to these claims discussed above, which overcome the rejections under 35 U.S.C. §112, second paragraph, Applicants respectfully submit that these claims are allowable also under 35 U.S.C. §102.

New claims

Claims 78-82 are new. No new matter has been added. Claims 78 and 82 are supported in the specification as filed *inter alia* in paragraph [0711] of the application as published as U.S. Patent Application Publication No. 2009/0088816. Claims 79-81 are parallel to claims 4 and 5 as originally filed.

Applicants respectfully submit that these new claims are allowable at least because they depend from allowable independent claims, as discussed above.

Applicants believe the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection raised by the Examiner. In view of these amendments and remarks, Applicants respectfully submit that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

Respectfully submitted,

/William H. Dippert/

William H. Dippert
Reg. No. 26,723
Attorney for Applicant

Dated: March 15, 2012

Eckert Seamans Cherin & Mellott, LLC
10 Bank Street
Suite No. 700
White Plains, New York 10606

Phone: 914-286-2813 (Direct)

E-Mail: WDippert@eckertseamans.com

APPENDIX A

Birmingham, A., "The arrangement of the muscular fibres of the stomach," Transactions of the Royal Academy of Medicine in Ireland, Springer London (1898)

THE ARRANGEMENT OF THE MUSCULAR FIBRES OF THE STOMACH.

By A. BIRMINGHAM, M.D., *Professor of Anatomy, Catholic University, Dublin.*

A SHORT time ago, when making a careful dissection of a stomach, in which the muscular fibres were particularly well developed, I was surprised to find that the arrangement of these fibres differed in several important details from the descriptions found in all our text-books, I believe, without exception. My attention having been directed to the matter, I examined a number of stomachs; and as each corroborated the evidence of the first, I have come to the conclusion that our current descriptions of the muscular coat of this organ are at variance with the facts which can be brought out by a careful dissection in any ordinary stomach the muscular coat of which is fairly well developed, particularly if it has not been artificially thinned-out by post-mortem over-distension, for the purpose of facilitating dissection, or otherwise.

As an example of the text-book descriptions, I shall give a summary of the account of the muscular coat found in the tenth edition of *Quain's Anatomy*, with which account, I may add, our other text-books practically agree.

Quain's description is as follows:—The muscular coat consists of three sets of fibres disposed in layers, and named from their direction the longitudinal, the circular, and the oblique fibres.

The longitudinal fibres are continuous with those of the œsophagus; they spread in a radiating manner from the cardiac orifice, and are found in greatest abundance along the curvatures, especially the lesser one. On the anterior and posterior surfaces they are thinly scattered or scarcely to be found, but are well marked, and form a thick uniform layer near the pylorus.

The circular fibres form a complete layer over the whole extent of the stomach. "They commence by small and thinly scattered rings at the extremity of the great cul-de-sac, describe larger and larger circles as they surround the body of the

stomach at right angles to its curved axis, and towards the pyloric end again form smaller rings, and at the same time become much thicker and stronger than at any other point. At the pylorus itself they are gathered into a thick bundle, which forms, within a circular fold of mucous membrane—the pyloric sphincter. Some of the circular fibres appear to be continued from those of the œsophagus, spreading from its right side."

"The innermost muscular layer is incomplete, and consists of the oblique fibres. These are continuous with the circular fibres of the gullet, on the left of the cardiac orifice, where they form a considerable stratum; from that place they descend obliquely on the anterior and posterior surfaces of the stomach, where

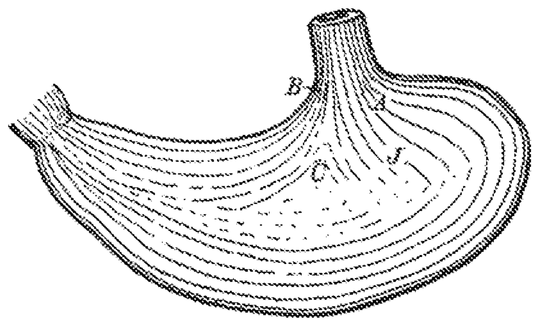


FIG. 1.—Outer layer of muscular coat of stomach. The longitudinal fibres of the front of the œsophagus are seen passing at *A* towards the fundus, and on to the great curvature, at *B* on to the lesser curvature, and at *J* blending with the underlying fibres of the middle layer. The fibres of this outer layer form a continuous covering all over the greater part of the stomach, but in the region marked *C* they are irregularly disposed or wanting.

they spread out from one another, and, taking the direction of the circular fibres, gradually disappear on the greater curvature."

Taking as the basis of my description the usual division of the muscular coat into three layers—an outer, a middle, and an internal—I have invariably found in stomachs suitable for a proper dissection of this coat the following arrangement, which is, I would submit, the true disposition of these layers.

The Outer, or Layer of Longitudinal Fibres.—As regards these fibres I have little to say that does not agree with the usual accounts in our text-books. Its fibres are, of course, continuous with the longitudinal fibres of the œsophagus, and they form on

each curvature, but particularly on the lesser, a well-marked layer of numerous distinct bundles, which thin off as the two surfaces are reached. The layer exists, nevertheless, all over the greater part of these surfaces as a very thin sheet, the fibres being less distinctly longitudinal in places—particularly near the middle of the surfaces beneath the cardia—than in the neighbourhood of the curvature (C, fig. 1). The fibres from the right side of the œsophagus pass along the lesser curvature; while those from the left side can be traced over the summit of the fundus, and along the great curvature to the pylorus, some distance from which the fibres of the two curvatures, spreading out, meet and form a continuous and well-developed layer, of nearly equal thickness all round the narrow end of the stomach. The fibres on the front and the back of the œsophagus pass to the corresponding surfaces of the stomach, some arching towards the right, and others, which are much more numerous, towards the left. These latter, as they run downward and to the left, become mixed—to a greater extent than would appear on viewing the surface of the outer layer—with the underlying fibres of the next layer, which at this part of the stomach are passing in an almost similar direction (J, fig. 1; N, fig. 2). Between these œsophageal fibres sweeping to right and left, there is an area on each surface some distance below the cardia in which the fibres of this layer are irregular or wanting.

Fig. 1 gives a good idea of the general arrangement of the layer, but it should be pointed out that many of the fibres at J in fig. 1, which appear to be continuous with the longitudinal fibres of the œsophagus, really belong to the middle layer, as can be shown by pulling off the longitudinal fibres descending from the œsophagus.

The Middle Layer.—The fibres of this layer are said—as shown in the quotation given above—to commence in the form of circles at the fundus, and to extend as a series of rings surrounding the stomach in its whole length as far as the pylorus, where they are thickened to form the pyloric sphincter. With this description I cannot agree. An obvious objection to such a description of the layer—apart from the fact that such an arrangement cannot be shown by dissection—is the difficulty, or impossibility, of tracing the continuity between fibres so disposed

and the circular fibres of the œsophagus,—a difficulty which is got over in some descriptions by avoiding the question altogether, and simply stating that the fibres of the internal or oblique layer are continuous with the circular fibres of the œsophagus, while the circular fibres are allowed to commence on their own account at the fundus, no connection of any kind with the œsophagus being mentioned.

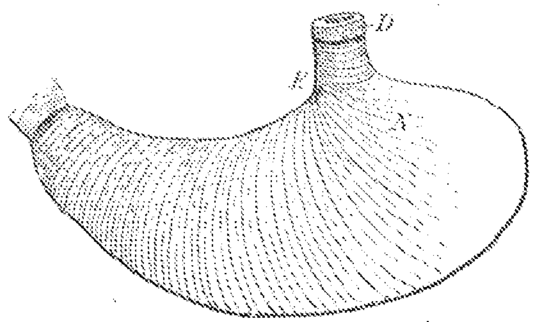


FIG. 2.—Middle layer of muscular coat of stomach. *D*, some of the outer longitudinal fibres of the œsophagus which are removed lower down, showing the superficial set of the circular fibres; these pass at *E* into the fibres of the middle layer of stomach. *N*, the oblique fibres of the middle layer, which blend to some extent with the overlying fibres of the outer layer (see *J*, fig. 1).

The current description, as quoted above, is practically correct in so far as it relates to the portion of the layer which lies to the right of the œsophagus. That part of it, however, which refers to the portion of the layer on the left of the œsophagus is entirely inaccurate, for the very simple reasons that practically no fibres of the layer, at least no annular fibres, are found to the left of the cardia, and the fibres which form rings around the wide end of the stomach, commencing at the fundus, really belong to the internal or oblique, not to the circular layer of the muscular coat.

The arrangement of the fibres of this coat will be most easily understood if we take up their description at the pyloric end, and follow them towards the opposite extremity of the stomach.

At the pylorus, as usually described, the circular fibres are numerous and well developed, constituting the pyloric sphincter, which surrounds this aperture in the form of a distinct and stout muscular ring. In the adjacent narrow portion of the stomach

the fibres are also well developed, and the resulting rings are numerous and closely placed. As we pass on towards the left the layer becomes thinner and the rings correspondingly fewer, but they still form a distinct and well-defined continuous sheet, the fibres of which can be easily seen, even through the peritoneum, forming very symmetrical rings, disposed at right angles to the long axis of the organ. This regular arrangement is continued as far as the region of the œsophagus, where it is interrupted. Here the upper portion of the rings, as they cross the lesser curvature of the stomach, 'hitch' against the termination of the œsophagus, and are prevented, as it were, from passing any farther to the left, whilst the lower portions of these fibres —namely, those on the surfaces—radiate from the right side of the cardia (where they are more or less heaped up against the œsophagus) downwards and to the left, with varying degrees of obliquity, across the surfaces of the stomach. They finally end on these surfaces a little to the left of the line of the œsophagus, where they blend with the overlying longitudinal fibres passing downwards and to the left from the front of the œsophagus, and, in part at least, turn down towards the great curvature and join the underlying circular fibres of the internal layer—a termination similar to that of the oblique fibres of the internal layer (fig. 2). These fibres of the middle layer, which I have just described as radiating from the right side of the œsophageal orifice, pass by a gradual transition on the right side into the ordinary circular rings of the stomach, without any sudden change in their direction (fig. 2); whilst tracing them onwards towards the left they will be found to become gradually more oblique, passing from the right edge of the cardia to higher and higher positions on the two surfaces, until, finally becoming horizontal (E, fig. 2), they pass into the most superficial of the circular fibres of the œsophagus.

This arrangement can be reproduced diagrammatically by taking a distended stomach with a portion of the œsophagus attached, and passing on to it, over its pyloric end, a large number of elastic rings to represent the circular fibres. In the neighbourhood of the pylorus and the adjacent parts of the stomach the rings should be disposed in a continuous series at right

angles to the long axis of the stomach, until the œsophagus is reached. The next ring after this having been passed over the pyloric end, should be drawn across the stomach until its upper end is caught by the œsophagus, its lower end should be then moved a little way towards the fundus; the succeeding ring having been carried as far as the œsophagus above, should have its lower end drawn still further to the left, and so on, until finally a ring is put on which, when its upper end hitches against the œsophagus, has its lower end carried to the left, right over the fundus, so that it will come to lie as a band around the termination of the œsophagus (fig. 2).

It should be added that, unlike the elastic bands in the arrangement just described, the fibres which radiate from the right side of the œsophagus downwards and to the left across the two surfaces of the stomach do not form complete rings, but that, having blent to some extent with the overlying prolongations of the longitudinal fibres of the œsophagus on the front and back of the stomach (which are running in the same direction), and to a slight extent with the circular fibres of the internal layer, they become lost on the surfaces, and cannot be followed to the region of the great curvature.

The Internal Layer.—As I traced the circular fibres from the pylorus, I may, for convenience, trace these fibres from the fundus, for they are arranged on the portion of the stomach which lies to the left of the œsophagus, in practically the same manner as the circular fibres are arranged on the portion of the stomach to the right of the œsophagus. They begin as circles at the summit of the fundus (I., fig. 3), whence, forming larger and larger circles, they pass to the right in the form of rings encircling the wide end of the stomach, and disposed at right angles to the long axis of this part of the organ. When they reach the left side of the œsophagus the upper ends of the rings 'hitch' against it (an arrangement similar to that described on the opposite side of this tube in connection with the middle layer), whilst the rest of the rings radiate with increasing degrees of obliquity from the left side of the cardia across the two surfaces, as the well-known and commonly-described 'oblique fibres' of the stomach (fig. 3). Of these oblique fibres those nearest to the fundus run with a very slight degree of obliquity,

for the transition from the fibres which form rings round the wide end of the stomach to the well-known oblique fibres is very gradual. The next fibres are more distinctly oblique, and are carried a considerable distance towards the pyloric end, whilst the succeeding and highest fibres run nearly parallel to, and no great distance from, the lesser curvature, reaching almost as far as the antrum pylori. Above this (K, fig. 3) the oblique

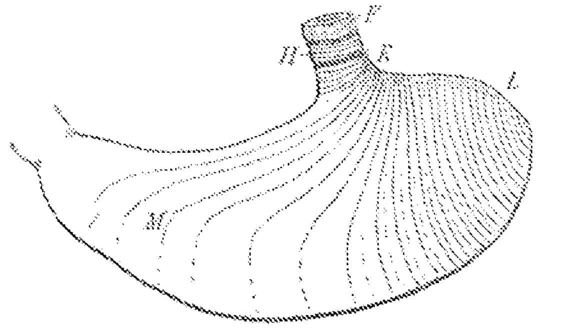


FIG. 3.—Internal layer of muscular coat of stomach. *F*, longitudinal fibres of œsophagus, removed at *H* to show the superficial set of circular fibres. *K*, deep circular fibres of the œsophagus passing below into continuity with fibres of internal layer of stomach. *L*, fibres of internal layer forming rings round fundus. *M*, oblique fibres of internal layer, ending by turning abruptly towards great curvature, and passing into circular fibres of the overlying middle layer.

fibres are continuous with the deeper circular fibres of the œsophagus.

It should be pointed out here that the circular fibres at the termination of the œsophagus are divisible into a superficial set continuous with the fibres of the middle layer of the stomach, which radiate from the right side of the cardia, and a deep layer, which are similarly continuous with the oblique fibres of the internal layer. Not that these two sets of the circular fibres are distinctly separated from one another in the œsophagus, but it will be found, on removing the longitudinal fibres at the lower end of the tube, that the circular fibres lying immediately beneath assume, as the stomach is approached, an oblique direction, as if the left end of the rings which these fibres form were slipping down at that side of the tube on to the stomach; below this they are seen to be continuous with the fibres of the

middle layer of the muscular coat (E, fig. 2). If these superficial circular fibres just described be removed, it will be found that there lies beneath them another set, the deeper circular fibres, which becoming oblique in the opposite direction, slip down along the right margin of the œsophagus as the stomach is approached, and pass into the oblique fibres of the internal layer of the stomach (K, fig. 3).

It will be remarked that in both the middle and internal layers circular and oblique fibres are found. The *circular* fibres surround all of the stomach to the right of the œsophagus in the middle layer, all to the left of the œsophagus in the internal layer, the *oblique* fibres of the middle layer radiate from the right margin of the cardia downwards and to the left, whilst in the internal layer they radiate from the left margin of the cardia downwards and to the right, in each case on both surfaces of the stomach.

The termination of the oblique fibres of the internal layer, I found, corresponded to the description given in our text-books. They all, so far as I could make out, after passing across the surfaces of the stomach obliquely for variable distances, turn rather abruptly towards the great curvature and join the circular fibres of the middle layer (M, fig. 3). As pointed out above, at least some of the oblique fibres of the middle layer terminate in a corresponding fashion.

SUMMARY.

The muscular coat of the stomach consists of three incomplete layers—External, Middle, and Internal.

1. *The External Layer* consists, as usually described, of longitudinal fibres continuous with those of the œsophagus, best marked on the lesser curvature when the stomach is distended, also well seen on the great curvature and near the pylorus, but represented in practically all other parts by a thin layer, the fibres of which are irregular on the two surfaces below the cardia.

2. *The Middle Layer* is composed of circular and oblique fibres: the former, which are the more numerous, are found in the form of rings surrounding the stomach from the sphincter pylori,

which they form, to the cardia. Beyond this the layer is continued for some distance in the form of oblique fibres, which radiate from the right side of the œsophageal opening above, downward and to the left on the two surfaces of the stomach. These fibres, becoming more and more oblique, are continued above into the superficial circular fibres of the lower end of the œsophagus. The fibres of this layer do not, as usually described, encircle the wide end of the stomach with a series of rings; these rings belong to the next layer.

3. *The Internal Layer* is composed, like the middle layer, of circular and oblique fibres; but whilst the oblique fibres are but slightly developed in the middle layer, they form an important part of the internal layer. Beginning as a series of circles at the summit of the fundus, it extends in the form of a layer of rings, disposed at right angles to the axis of the stomach, as far as the cardia. Beyond this it is continued by a number of fibres—the well-known oblique muscular fibres of the stomach—which radiate from the left side of the œsophageal opening, downwards and to the right on both surfaces of the stomach, some of them reaching almost as far as the antrum pylori. These fibres end by turning abruptly towards the great curvature and passing into the circular fibres of the middle layer. The highest of these oblique fibres pass above into the deeper circular fibres of the œsophagus.

APPENDIX B

Bilgutay AM et al., " Gastro-intestinal Pacing: A New Concept in the Treatment of Ileus," Ann Surg. 1963 September; 158(3): 338–347

Gastro-intestinal Pacing: *

A New Concept in the Treatment of Ileus

Aydin M. Bilgutay,** M.D., Robert Wingrove, B.E.E., Ward O. Griffen,*** M.D., Raymond C. Bonnabeau, Jr.,** M.D., C. Walton Lillehei, Ph.D., M.D.

From the Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

Paralytic ileus is a form of intestinal obstruction characterized by inadequate peristaltic activity affecting the gastro-intestinal system in its entirety or segmentally. Loss of normal peristaltic activity frequently occurs following intra-abdominal surgery, and secondary to a variety of pathological conditions such as peritonitis of various etiologies, retroperitoneal sepsis and hemorrhage, and from trauma, infections, or surgery in areas remote from the abdominal cavity. Spinal injuries, diseases or the genito-urinary tract, and thoracic surgery or trauma are frequently observed causes of paresis of the bowel occurring as a reflex inhibition. Loss of effective peristaltic activity of the gastro-intestinal tract rapidly leads to distention of bowel loops with fluid and gas, which if left untreated is prone to perpetuate itself as a vicious cycle, the more distention occurring the more paralyzed the bowel becomes. Fluid and electrolytes are lost into this third space and distention of the intestine further impairs absorption. In addition, distended inactive loops may twist or kink and a mechanical obstruction thus may be superimposed.

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*** Markle Scholar in the Medical Sciences.

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Management of this condition heretofore has been largely passive in nature and has not changed significantly since introduction of nasogastric intubation and suction [13] with administration of intravenous fluids and electrolytes continued until the paretic bowel resumes its tonus and peristaltic activity. Hypertonic saline, multiple enemas, spinal anesthesia, repeated use of hot stupes to the abdomen, and bowel stimulants such as prostigmine, neostigmine, pitressin, and pantothenic acid have all been used with variable and inconsistent success.[14]

The purpose of this presentation is to introduce a new concept in the treatment of paralytic ileus by direct electrical stimulation of the gastro-intestinal system utilizing a specially designed electronic pacemaker (Fig. 1).

Development of the Gastro-intestinal Pacemaker

Open-heart surgery for ventricular septal defects, tetralogy of Fallot, and atrioventricularis communis types of septal defects was introduced in 1954.[8, 15] Postsurgical complete heart block with its slow rate was experienced in some of these patients. It quickly became apparent that the then available methods for treatment by means of drugs or externally applied electric shocks were entirely inadequate for increasing cardiac output and consequently the mortality rate in the blocked patients was very high. Experimental investigation upon

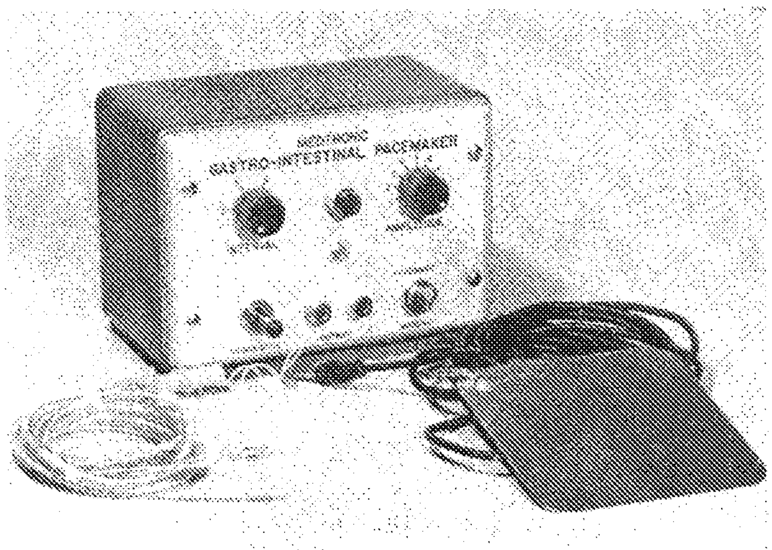

FIG. 1. Equipment for gastro-intestinal pacing. Variable rate and amplitude pacemaker, gastric tube electrode, and indifferent plate electrode.

the feasibility of direct stimulation via a myocardial electrode was begun upon the premise that cardiac muscle forms a true syncytium and that a direct stimulus to a muscle fiber in the ventricle of the heart results in a contraction of the entire organ. This avenue of investigation did prove fruitful and significantly altered treatment and prognosis of complete heart block.[16, 17]

In contrast, in striated muscle only the fiber stimulated will contract. The behavior of the gastro-intestinal muscle, on the other hand, lies midway between that of the myocardium and striated muscle. If one stimulates a point upon the small intestine either mechanically or electrically, a local contraction results which usually is propagated for a short distance from the point of stimulation. Sometimes, however, stimulation at a point will produce a peristaltic rush which will traverse a considerable length of the intestine. Thus, intestinal muscle also behaves as a syncytium but is not *all or none* in its response. Anatomically it is not certain whether the fibers of intestinal muscle communicate with each other or not. They appear to be quite discrete. However, any connections that may exist seem to be unimportant since it is known that conduction does result from the passage of electrical activity directly from active to inactive contiguous smooth muscle cells as well as via the diffuse intrinsic nervous network (plexus of Auerbach and Meissner[5]).

The striking success of electrical cardiac pacemaking via myocardial electrodes in the treatment of complete heart block[16, 17] together with the analogous functional factors just mentioned suggested the possibility of application of a similar concept to the treatment of abdominal distention due to inadequate peristalsis by stimulating gastro-intestinal motility by means of direct pacing.

Exploratory observations upon dogs indicated that this concept was basically sound and worthy of further investigation.

Our initial experiments upon the dogs' gastro-intestinal motility were designed to find optimal current amplitudes, pulse length, frequency, and to determine feasible sites in the gastro-intestinal tract for effective stimulation. Extensive experiments followed with various types of current in regard to wave-shapes, pulse length, and frequency and with regard to their effectiveness in inducing peristaltic activity. These were then tested and modified for human use based on experiments carried out on the authors under fluoroscopy and

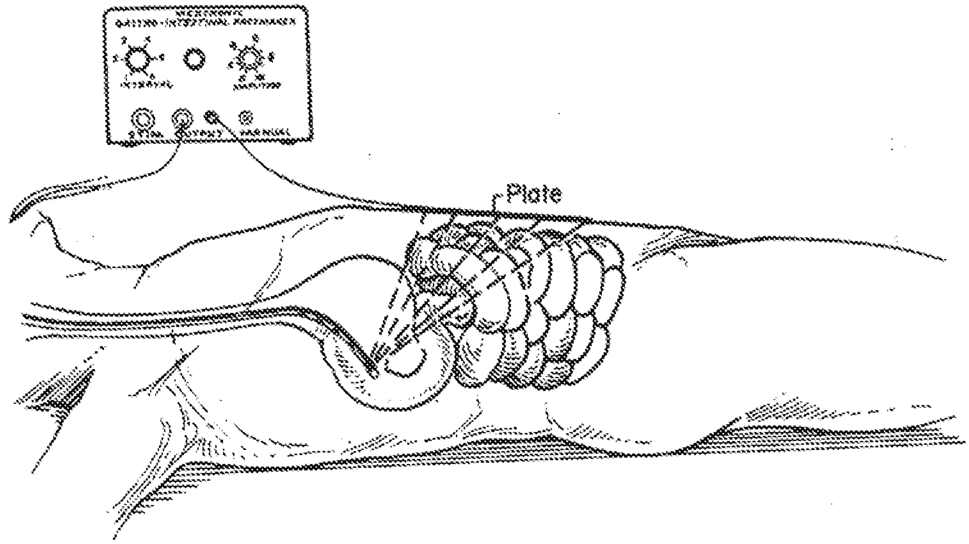

Fig. 2. Technic of gastro-intestinal pacing. Tube electrode is introduced nasogastrically into the stomach and can serve a dual purpose, suction and stimulation. The indifferent plate electrode is applied to the abdominal wall. If operative incisions, colostomies, and dressings do not permit application of the indifferent electrode to the ventral abdominal wall, flanks or dorsal abdominal wall can be utilized. Both electrodes are then connected to the gastro-intestinal pacemaker which is set to deliver impulses at one minute intervals. Other effective routes of stimulation are via a rectal electrode or direct attachment of the electrodes to the bowel.

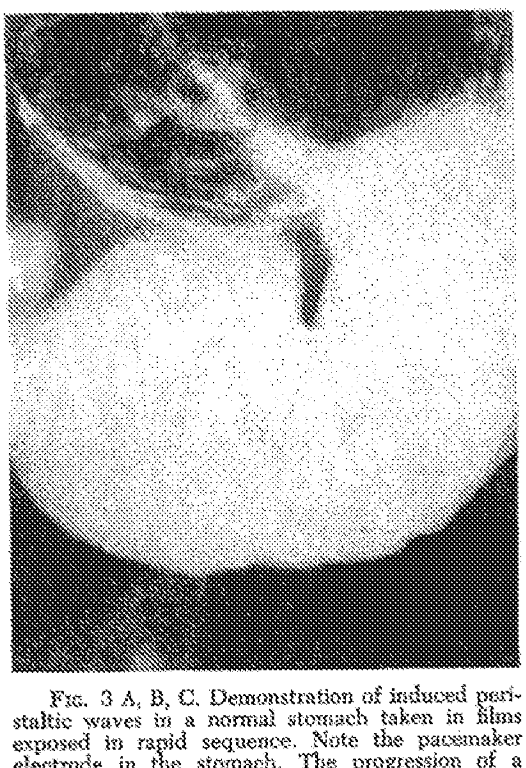

Fig. 3 A, B, C. Demonstration of induced peristaltic waves in a normal stomach taken in films exposed in rapid sequence. Note the pacemaker electrode in the stomach. The progression of a peristaltic wave can be readily followed in the series.

Figure 3B.

later in the operating room by direct observation upon patients undergoing laparotomy (Fig. 3).

It was found from these studies that a current of 7.0 to 10 MA (milli-amperes) output and a frequency of 50 cycles/sec. given for five to 10 seconds duration would be sufficient to induce effective peristaltic activity and was not perceptible to the patient. Hence, a pacemaker was designed with variable output (1–10 MA) equipped with a timer to give impulses of 50 cycles/second of pulsating current of five seconds duration at adjustable intervals from one to five minutes (Fig. 1).

Along with these studies, determination of sites for effective stimulation was also the stomach, pylorus, and first, second, and carried out. Fundus, corpus, and antrum of third portions of the duodenum were stimulated with different types of current. While responses were obtained from all these areas, most effective peristaltic waves appeared when the antrum and first and second parts of the duodenum were stimulated.

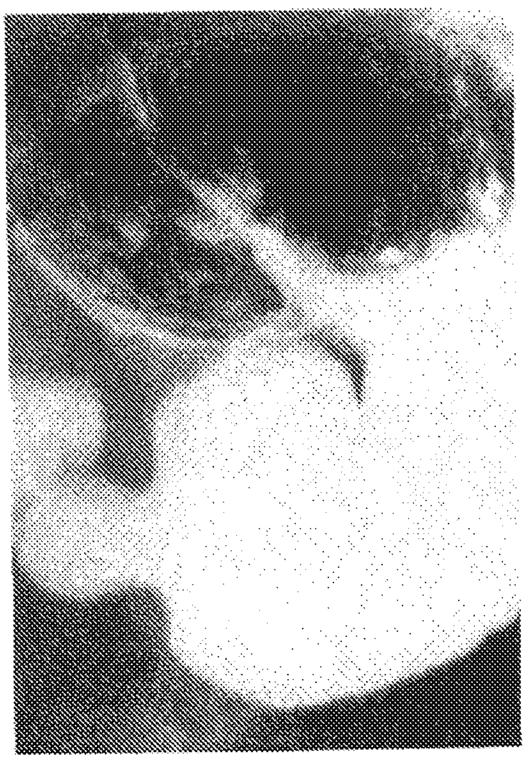

FIGURE 3C.

Stimulation was tried by unipolar and bipolar electrodes, intraluminally, transluminally, intramurally, and via the serosa. Unipolar, transluminal stimulation was favored and accepted for clinical application because of convenience and because it was reasoned that the electrical field created by the use of unipolar electrodes would traverse the whole thickness of the bowel wall and stimulate both Meissner's and Auerbach's plexus and the smooth muscle layers over a larger area (Fig. 2).

Technic

The following method was developed for clinical gastro-intestinal pacing. A specially designed brass tip electrode was incorporated onto a standard plastic disposable nasogastric tube (Fig. 1) and passed into the stomach transnasally and advanced to lie in the antral region. The indifferent electrode in the form of a 5 × 5-inch plate (Fig. 1) is taped on either the ventral or dorsal abdominal wall. Both electrodes are then connected to the gastro-intestinal pacemaker which is set to deliver impulses at set intervals (Fig. 2). As the gastric activity is greatest normally in the antrum where trituration, mixing, and emptying are effected, we prefer to stimulate this more active area. In patients with ileus, pacing is continued until gas and the first stool is passed.

The rectal route wherein an electrode probe is passed into the rectum has also been used clinically for stimulation. This method was initially tried to evacuate the large bowel (electrical enemas), but has been found feasible for inducing peristalsis to paretic bowel postoperatively. Intramural implantation or serosal attachment of bipolar electrodes to the stomach wall by catgut stitches at the time of surgery with the lead wires brought out through a tiny stab wound in the abdominal wall

has been utilized effectively for stimulation in experiments.

Clinical Application

To date, gastro-intestinal pacing has been utilized in over 40 patients with paralytic ileus of differing etiologies. Reports of representative patients treated follows:

Case Reports

Postoperative Use

Case 1 (E. M., U. H. 995834). This 62-year-old white woman was admitted to the University of Minnesota Hospitals with complaints of pyrosis and dysphagia. She had been a chronic alcoholic for 27 years. Her esophagogram showed an esophageal stricture near the cardia with a large hiatus hernia. Esophagoscopy revealed a peptic ulcer at the strictured area. She had 60-degree free acid upon histamine stimulation. On December 10, 1962, she underwent laparotomy for repair of the hiatus hernia with coincidental vagotomy and pyloroplasty. Postoperatively, transgastric gastro-intestinal pacing was started utilizing a current of 10 MA with impulses of five seconds duration delivered every minute. Active bowel sounds could be auscultated during stimulation. Sixteen hours after pacing started, she passed gas and had a bowel movement at which time pacing was discontinued and oral intake started.

Comment. In this case and in five other patients who had had either Billroth II or segmental gastrectomy with pyloroplasty and bilateral vagotomy, transgastric, rectal or gastro-intestinal pacing was effective in inducing and maintaining bowel motility. In these cases it required an average of 16 hours of pacing before the first stool was passed, following which pacing was routinely discontinued. These patients have demonstrated that peristaltic activity could be induced and maintained by pacing and the period of recovery of function for the paretic bowel could be shortened after gastric resections with vagotomy and pyloroplasty.

Case 2 (B. C., U. H. 920698). This 8-year-old white girl had biliary cirrhosis, portal hypertension, and repeated episodes of hemorrhage from esophageal varices since the age of one month. She was admitted at this time because of another episode of massive bleeding. Following attempted nonoperative management she underwent laparotomy on December 12, 1962. A splenectomy, splenorenal shunt, and liver biopsy were performed. Twelve hours postoperatively it was noticed that she had developed a severe thrombophlebitis at her cutdown site in the leg. Other cutdown sites in the legs and arms had been utilized on previous admissions for the episodes of bleeding. In order to permit starting her on oral fluids early, gastro-intestinal pacing was started transrectally utilizing a current output of 10 MA of five seconds duration with impulses every minute. This route was chose as it was not deemed feasible to pass the electrode into the stomach for fear that her varices might be further traumatized. Oral intake was well tolerated. Nasogastric suction was discontinued. Within 16 hours after initiation of gastric pacing she had five stools and was therefore advanced on oral intake and pacing was discontinued.

Comment. This case illustrates the feasibility and advantages of rectal stimulation in certain patients, and also the early commencement of oral intake facilitated recovery in this patient with a complicated surgical problem and in a debilitated condition preoperatively.

Case 3 (E. E., U. H. 870212). This 44-year-old white woman with rheumatic heart disease (mitral insufficiency, mitral stenosis, aortic insufficiency, aortic stenosis) was admitted with complaints of severe right lower quadrant pain, anorexia, and vomiting. She was initially treated nonoperatively, but during the next 48 hours an increase in intensity of the right lower quadrant pain, development of rebound tenderness, and a rise in her white blood count occurred, and therefore she was explored on December 9, 1962. At laparotomy she was found to have acute oophoritis. Cholecystectomy and appendectomy were also performed after careful exploration of the small bowel. Six hours postoperatively, transgastric gastro-intestinal stimulation was started. A current output of 9 MA for five seconds duration was delivered every minute for gastro-intestinal pacing. Nasogastric suction was discontinued and oral fluids were allowed. She experienced no nausea or vomiting. During stimulation, she volunteered the information, "my stomach is rumbling." She started to pass gas and had a bowel movement in 12 hours upon which pacing was discontinued.

Comment. In this patient, no nasogastric suction was employed and there was no

need to replace fluids or electrolytes which would have been lost by suction. Oral intake was allowed and recovery was shortened without prolonged requirement for intravenous administration of fluid and electrolytes. Moreover, the dangers of electrolyte imbalance in a patient with low cardiac reserve and on digitalis therapy were obviated. Return of spontaneous peristaltic activity has been achieved in similarly short times following other abdominal operations including colectomies and resection of abdominal aneurysms.

Case 4, F. G. This 66-year-old white man was admitted to the University of Minnesota Hospitals with constant right upper quadrant pains of five days duration. He had had a cholecystostomy 18 years ago. However, since then he had belching, flatulance, and fatty fried food intolerance. At the present admission, he had jaundice with a bilirubin of 4.0 mg.%. On February 8, 1963 a common bile duct exploration was carried out. A duodenotomy, sphincteroplasty, and cholecystectomy were also performed. His early postoperative recovery was smooth. He was started on a regular diet on February 16, 1963. The next day he started vomiting and belching with recurrence of epigastric distress and abdominal distention. This situation continued until February 21, 1963 when an upper gastro-intestinal series was obtained and a hugely dilated stomach with near total obstruction of the gastric outlet was revealed (upper gastro-intestinal series 2 weeks prior to this was normal). Intramural hemorrhage incident to duodenotomy and sphincteroplasty, an acute ulcer with spasm, and a right upper quadrant abscess with ileus were some of the conditions entertained as possible mechanisms to explain the gastric outlet obstruction. On February 23, 1963, a milk drip of 150 cc./hour with 10-minute aspirations every hour was started. On this regimen return of gastric aspirates varied between 120 and 280 cc. every hour. Exploration was considered, but in reviewing the x-rays the possibility of a gastric atony and dilatation were considered as possibly a primary condition rather than being secondary to obstruction. Gastro-intestinal pacing therefore was started. Fluoroscopic and cinegraphic study of the stomach was also carried out. While the stomach stayed atonic and dilated for one-half hour during observations under fluoroscopy, it readily exhibited peristaltic activity upon pacing and emptied into the duodenum. Pacing was continued over the next day with the same amount of milk drop hourly. The gastric aspirations decreased in amount to 45 to 12 cc. every hour. Pacing was discontinued on March 2, 1962 and the patient was discharged without resort to exploration.

Comment. This case illustrates the use of gastro-intestinal pacing both diagnostically and therapeutically. Its use here undoubtedly eliminated re-exploration. The use of gastro-intestinal pacing in diagnostic radiology to detect abnormal areas of rigidity, fixation, or displacement may not only help with the evaluation, but also shorten the time of exposure to radiation.

Ileus Secondary to Renal Colic

Case 5 (K. E., U. H. 999764). This 33-year-old white man was admitted to the University of Minnesota Hospitals on March 4, 1963 with a three-day history of colicky left flank pain and hematuria for two days. He had not been able to pass stools and had been nauseated, vomiting, and not eating for the prior three days. Past history revealed that he had had renal stones diagnosed six years ago, and he had been having intermittent attacks of renal colic from time to time. On admission, his abdomen was distended and silent. A flat film of the abdomen revealed a kidney stone in the left kidney pelvis and ileus. The entire gastro-intestinal system was dilated with gas. Transgastric pacing was started on March 5, 1963 at 3:00 p.m. with immediate return of bowel sounds. Oral fluids were allowed. After a few hours the patient stated he felt more comfortable. The nausea, vomiting, and crampy abdominal pain had disappeared. He started passing gas 12 hours later and then had a bowel movement. The next day he was operated upon for removal of his kidney stone (Fig. 4).

Comment. This case illustrates effective management of reflex ileus secondary to kidney stone by gastro-intestinal pacing. Reflex inhibition of peristaltic activity in the dilated bowel can be counteracted by pacemaker stimulation.

Discussion

Wangensteen[14] has emphasized that *paralytic ileus* is an ill-chosen name for the meteorism and motor inactivity of the bowel frequently observed in the numerous clinical situations in which this condition is evident.

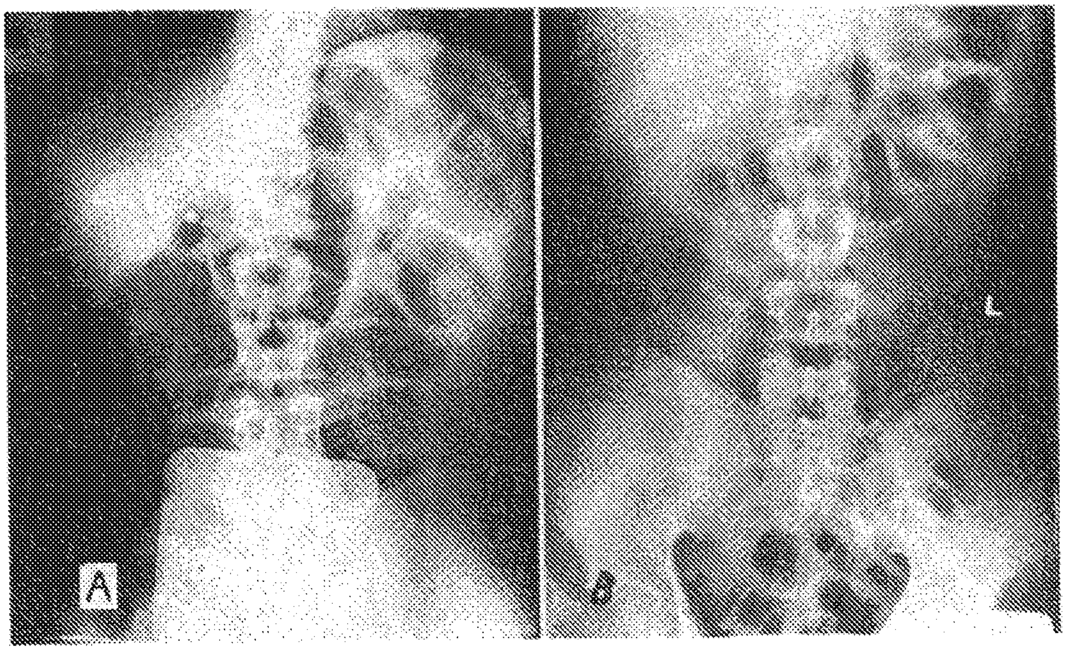

FIG. 4. Abdominal x-rays of Patient K. E. with reflex ileus secondary to renal stone and colic. A. X-ray taken upon starting gastro-intestinal pacing. Note distended bowel and position of the electrodes. No suction was utilized. Oral intake was allowed. Left renal calculus is shown. B. Twelve hours later. Patient passed flatus and feces. Film shows decreased gas and distention.

Numerous observers have provided evidence that the intestine is not paralyzed, rather its activity appears to be inhibited and restrained but it does remain responsive.

In chemical iodine peritonitis, Frey[8] observed the intestinal activity through a celluloid window and found that dilated and contracted segments responded similarly to stimulation with choline given subcutaneously. In the intestines distended with gas for several hours, Hotz[9] found that the rhythmic contractions of the segment ceased. The gaseous distention of the loop and not the toxins of peritonitis, Hotz concluded, were responsible for the disappearance of intestinal contractions. Distention of the intestine impairs absorption and the gas in the intestine which is normally carried away as fast as it is formed, continues to accumulate and a vicious cycle ensues.[11, 18]

The degree of intestinal distention and fluid accumulation in paralytic ileus varies greatly; but when extreme or protracted may be a fatal complication.

We have observed in these studies that the gastro-intestinal system remains responsive to pacemaker stimulation in dogs subjected to the effects of atropine, bilateral vagotomy, after gastrectomies (Billroth I, II, segmental), after pyloroplasties, after induced bile or septic peritonitis, and in mechanical obstructions. Hotz[9] showed, many years ago, that loops of intestinal musculature from animals suffering from peritonitis exhibited a fairly normal contractile power and the reaction to stimulation with drugs was normal.

In our patients, we have also observed that electrical pacemaking was successful in stimulating peristalsis in postoperative ileus following intra-abdominal operations including vagotomies, pyloroplasties, gastrectomies, procedures requiring wide retroperitoneal dissection, and also in reflex ileus. Clinically, it has usually required six to 20 hours (an average of 16 hours) of

stimulation before pacing could be discontinued in these conditions.

We have not yet completed a controlled clinical study * to determine and compare the time interval required before return of spontaneous peristaltic activity postoperatively wtih that observed when gastro-intestinal pacing has been utilized; however, this is less significant than the clear-cut observation that the function of the bowel can be promptly induced and maintained by pacing in a previously distended inactive intestinal tract.

The earlier return of bowel activity achieved when using gastro-intestinal pacing is utilized has reduced the time interval required for intravenous administration of fluids and electrolytes and the period of intubation has also been shortened or even eliminated. Oral intake is resumed sooner. As gastro-intestinal motility can be induced and maintained by pacing, swallowed gas or gas formed in the intestines is carried away by peristalsis.

However, a combination of nasogastric suction and pacing may usually be desirable at the start of therapy in cases with a full-blown picture of ileus. For this reason, we have incorporated the electrode for stimulation at the tip of an ordinary plastic disposable nasogastric tube to serve a dual purpose.

Clinicians are often troubled on occasion in making a differential diagnosis between a strangulating mechanical obstruction and paralytic ileus. Heretofore, in some patients differentiation has been impossible and operation of necessity carried out. Gastro-intestinal pacing offers promise in resolving some of these difficult problems. It is also interesting to speculate as to whether earlier return of motility in ileus associated with peritonitis might reduce the formation of adhesions.

Distention impairs absorption. Induced peristalsis is effective in carrying the intestinal gas away thus correcting or preventing distention which is a major factor responsible for impaired absorption. These circumstances may permit early oral intake in patients postoperatively. We have tried this in a number of our patients with success, by allowing oral fluids while they were being paced instead of resorting to intravenous fluids and nasogastric suction. Wider exploration of the feasibility of this method is under way.

Our experiments on dogs showed more forceful peristaltic activity in response to pacing when the stomachs were filled with liquids as judged both by direct observation and balloon pressure studies. Hunt and Spurrell[7] showed gastric emptying to be exponential in form and fundamentally dependent on the volume of gastric contents. Our findings support their observations. Not every peristaltic wave induced by pacing at the antrum crosses the pylorus. This simulates normal gastric motility and is explainable by enterogastric reflexes (neural or hormonal) which regulate gastric emptying.[4] It appears that the normal mechanism of gastric emptying is not altered by pacing. This is advantageous, as otherwise diarrhea might follow each meal or occur with pacing were each peristaltic wave conducted across the pylorus and traversed the entire bowel.

Morphine[3, 16] has a marked effect on lessening gastric motility and increasing the tonus of the pylorus interfering with the normal gastric emptying rate. With pacing peristalsis can be induced under the effect of morphine but gastric emptying is similarly retarded. Demerol (pethidine) has been reported to have virtually no effect on normal tone and peristalsis even in a fully effective dose.[18]

In the clinical studies reported, we have been following response to pacing by aus-

* To date, in this study of patients postoperative from all types of major surgical procedures, paced patients have shown return of peristaltic activity (passage of flatus) in an average of 20 hours as compared to an average of 55 hours in the non-paced group.

cultation of the abdomen for bowel sounds, and marking the time when patients would pass flatus and feces. When pacing is started immediately postoperatively, depending on the type of anesthesia and sedatives used and perhaps due to a decompressed stomach, bowel sounds may not be readily audible in the first few hours. However, as soon as patients are completely awake from anesthesia and intragastric contents are pushed into the duodenum by peristaltic waves that cross the pylorus and travel down the duodenum, typical peristaltic sounds are heard. When patients are allowed oral intake, this is more remarkable.

A pacemaker area has been described [5, 10] as being located in the second portion of the duodenum and controlling the activity of the small intestine somewhat similar to the sinus node in the heart. We have not, as yet, fully investigated the comparative efficacy of stimulation in this area, but have arbitrarily chosen the area of most marked activity in the stomach for stimulation of motility; namely, the antrum. As peristaltic waves are induced here and cross the pylorus and are carried down the duodenum, they will of necessity activate the duodenum which in turn, having a pacemaker area, thus stimulated, may control the rest of the intestinal tract. We have not proved whether gastrocolic reflex may be aroused by pacing via the stomach but return of peristaltic activity in the upper gastro-intestinal tract has been achieved by stimulation from the rectum.

Summary

Gastro-intestinal pacing has been introduced as a new concept for the active treatment of paralytic ileus.

Experimental development of a gastro-intestinal pacemaker and its clinical application has been described.

Indications, technic and advantages of gastro-intestinal pacing, both diagnostically and therapeutically, are illustrated in representative case histories.

Gastro-intestinal pacemaking shortens recovery from paralytic ileus, reduces or eliminates in some patients the need for nasogastric suction, intravenous fluids, and the dangers of induced electrolyte imbalances.

Acknowledgment

We would like to express our gratitude to Dr. Owen H. Wangensteen for his encouragement and advice.

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Discussion

Dr. Clarence Dennis (Brooklyn): My associate, Dr. Adrian Kantrowitz, has been working in this same field and is equally gratified with the experimental and clinical results which have been obtained. He has, however, embarked on some basic studies, to begin with, on the type of stimulus which is to be employed, whether it is a direct current stimulus or an alternating current stimulus; whether, if it is an alternating current stimulus, the frequency of cycles should be rapid or slow, or whether the shape of the wave of stimulus should be square wave, sine wave, or of what shape; and finally, the studies on the importance of the frequency of bursts of stimulation which take place.

Inasmuch as Dr. Bilgutay did not mention such basic studies in his presentation, I am very curious what his basic studies show in this regard.

Dr. C. Walton Lillehei (closing): There are relatively few cherished institutions left at Minnesota, but one that did seem almost invulnerable was use of the nasogastric tube with siphon drainage.

Nonetheless, I can emphasize, from our clinical experience to date, that this method of gastro-intestinal pacing is very effective. Exactly how far the method can go in eliminating the need for nasogastric intubation is not completely definable at this time. However, of the 45 patients treated to date referred to by Dr. Bilgutay in his presentation, a number required no gastric suction whatsoever during their postoperative interval. Others had suction with stimulation beginning immediately postoperatively for a period of time until they passed their first stool. In these postsurgical patients, this interval ranged from six to 24 hours with an average of 18 hours. At the time that they passed their first stool, pacing and intravenous fluids were discontinued and oral intake instituted.

The current that has been used for pacing in the clinical cases is provided by this small ($9 \times 6.25 \times 2.5$ cm.), self-contained battery powered unit called the Peri-Start which I am holding up. The large unit which you saw in the motion picture was our experimental stimulating unit which permitted us to vary the strength, type, and duration of the stimulating current. Extensive investigation has been done in our animal laboratory, and in humans under fluoroscopy and at operation with the abdomen open upon the types of current optimal for bowel stimulation. The results of those studies have allowed us to simplify this clinical unit (Peri-Start) because it does not need to be variable. The Peri-Start provides a current of 10 milliamperes at 50 cycles per second. The duration of the stimulus is 5 to 10 seconds, and it seems best if the stimulus occurs once a minute. A disposable nasogastric catheter electrode of polyvinyl plastic is provided for clinical usage.

In the motion picture just presented you were able to see the very prompt response of the gastro-intestinal tract to pacemaker stimulation in the dog with bile peritonitis. In fact, the induced contractions were identical to those occurring in the normal animal. It is interesting that in a paper in 1909 upon gastro-intestinal function, Hotz mentioned the fact that in his animal studies the bowel even though covered with pus from peritonitis was responsive to mechanical stimuli in virtually a normal manner, and that there was no real impairment in contractility unless distention took place. Distention is, of course, the most potent inhibitor of bowel motility. Therefore, often in ileus we do have a vicious circle of bowel distention due to swallowed and bacterial gas together with accumulation of the intestinal secretions further distending the bowel, this distention in turn increases the severity of the paresis and the entire cycle of bowel paralysis is kept in motion. Gastro-intestinal pacing, combined with a period of suction when